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CHANGES OF GAS METABOLISM, GAS HOMEOSTATIS AND TISSUE RESPIRATION IN RATS DURING PROLONGED HYPOKINESIA

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CHANGES OF GAS METABOLISM, GAS HOMEOSTASIS AND TISSUE RESPIRATION IN RATS DURING PROLONGED HYPOKINESIA

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The oxygen uptake and tissue gas homeostasis of restrained albino rats remained relatively constant during a 60-day experiment. The gas metabolism in some tissues changed, O_2 consumption increased in the liver and decreased in the myocardium. Capacity for physical work was reduced by 5 times. Hypokinesia for 60 days resulted in a delay in the animals growth.

Limited motor activity in man is one of the most important problems /1808* of our time. The latter is linked to the progressively increasing reduction in the volume of muscular work in all spheres of labor in the course of scientific and technical progress. The effect of hypokinesia on the organism is important also for clinical practice and space medicine.

In the numerous studies covering the general phenomenology and pathogenesis of hypokinesia considerable attention is given to the gas-energy aspect of hypokinesia [1-4, 8,9]. This is associated with the fact that a reduction in the level of muscular system functioning must inevitably alter the level of energy processes in the tissues, which in turn are in close relationship to the gas metabolism, dynamics of gasses on all levels of advance of O_2 and CO_2 in the organism.

*Numbers in margin indicate pagination in original foreign text.

The task of this study was a complex investigation of the general gas metabolism, intratissue gas homeostasis and intensity of tissue respiration in albino rats in the state of prolonged (60 day) hypokinesia.

Technique

Limited motor activity of experimental animals was induced by placing albino rats in special clamping cages where they were in a fixed pose for 60 days. The arrangement of the cages made it possible during the experiment to feed and water the animals, and remove wastes. The experimental and control rats were in one room under the same temperature conditions (+18-+20°); both groups were fed a diet of the Institute of Nutrition of the USSR Academy of Medical Sciences. In contrast to the experimental the control animals were placed in groups of 10 in cages of the usual vivarium type 45 x 45 x 35 cm in size. The general gas metabolism was determined by the method of closed chamber for 48 experimental and 30 control animals. For this purpose the group of rats (8-10) was placed for 1 h in a hermetically sealed thermostatically-controlled chamber at +20° of volume 0.17 m^2. The average total oxygen consumption, release of carbon dioxide (in ml for computation per 100 g of live weight in 1 min.) and respiratory coefficient (RC) were determined according to the final chemical composition of air (in %).

The intratissue pressure of oxygen (pO_2) and carbon dioxide (pCO_2) were determined according to the tissue depot method [11] in the modification of V. L. Popkov. The method we used of gas tonometry was based on the physical law of Henry-Dalton: pressure of gassesdissolved in the tissues is equal to the pressure of these gasses in a closed space above the tissue (in a gas depot). The constant gas depots in the subcutaneous cellular tissue are created by subcutaneous injection of 20 cm^3 of air. In 18 h 2-3 cm^3 of the gas mixture that had counterbalanced with the tissue was suctioned off by syringe for micro-analysis on a Skolender apparatus. The percentage composition of the gas mixture was recalculated for the pressure of oxygen (pO_2) and carbon dioxide (pCO_2) in mm Hg with regard for the total atmospheric pressure; the pressure of water vapors (pH_2O) and the temperature of the gas mixture in the depot. /1809

The intensity of tissue respiration was determined on the 45th and 60th day of hypokinesia on a Varburg apparatus in tissue sections of the large cerebral hemispheres, heart, liver and skeletal muscle (musculus quadriceps femoris). The sections were incubated in a Ringer-Locke solution in an atmosphere of pure oxygen [10].

At the end of the 60-day experiment in both groups of animals (experimental and control) the maximum physical performance capacity was determined according to the maximum time of swimming of the rats with a load equal to 15% of the animals weight (maximum dynamic work), and according to the maximum time for the stay of the animal on a vertical pole with cross notches (maximum static work). The correlation of free and phosphorylating oxidation (according to amytal-resistant and amytal-sensitive respiration) was studied by means of intra-abdominal injection of sodium amytal from a computation of 7 mg per 100 g of weight of the animal (according to the method of S. P. Maslov and I. N. Ivashkina [5]).

Study Results and Their Discussion

The studies indicated that the general gas metabolism in the albino rats during continuous 60-day stay in cages for limited movement was not significantly altered. As is apparent from the average data given in table 1, no significant changes were noted in the oxygen consumption during the experiment in the test and control rats. The release of carbon dioxide in the experimental animals somewhat exceeded that in the controls, which resulted in higher magnitudes of the respiratory coefficient, but its difference was statistically unreliable.

In addition to the determination of the general gas metabolism a study was made of the indices of intratissue gas homeostasis--pO_2 and pCO_2 (according to the method of gas depot). The oxygen pressure in the tissues is the final stage in the oxygen cascade on the path of O_2 entrance into the organism, and the tissue pressure of carbon dioxide characterizes the initial stage of CO_2 diffusion from the organism into the environment. The gas composition of the tissues has a great effect on the work of the

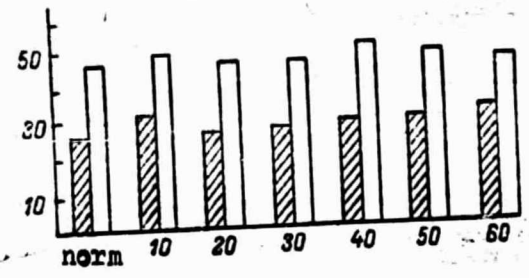
TABLE 1

GENERAL GAS METABOLISM OF ALBINO RATS IN 60-DAY HYPOKINESIA

Day of experiment	Control rats				Experimental rats			
	number of animals	mean consumption of O_2 in ml/100 g weight/1 min	mean release of CO_2 in ml/100 g of weight/1 min	respiratory coefficient	number of animals	mean consumption of O_2 in ml/100 g weight/1 min	mean release of CO_2 in ml/100 g weight/1 min	respiratory coefficient
Initial gas metabolism	30	3.10	2.18	0.72	48	3.03	2.08	0.68
15th	30	2.97	2.32	0.78	48	3.11	2.64	0.84
30th	30	3.27	2.28	0.69	46	3.24	2.68	0.82
45th	30	2.91	2.12	0.72	39	3.11	2.65	0.84
60th	30	2.83	2.43	0.85	23	2.98	2.66	0.89

enzymes, and consequently, on the course of metabolic processes in the tissues of the organism. As is apparent from the figure, the absolute amounts of pO_2 and pCO_2 in the subcutaneous gas depots during hypokinesia were not significantly altered. Analysis of our experimental data, according to Student, showed that the oscillations in pO_2 and pCO_2 in the tissues in the course of the experiment did not go beyond the limits of a confidence interval ($\bar{x} \pm 1.96\ \sigma_{\bar{x}}$) for the initial level; differences were not noted in the amounts pO_2 and pCO_2 in the experimental and control animals ($d>0.10$). In our opinion the oscillations in the intratissue pO_2 and pCO_2 are linked to the normal rhythm of the organism vital activity. Since the absolute amount pO_2 and pCO_2 in the peripheral tissues is a final result of the coordinated activity of the respiratory, circulatory and other systems of the organism, then based on the findings one should conclude that the system of oxygen and carbon dioxide transport in the organism in hypokinesia is not changed. /1810

In addition to the general gas metabolism it was also important to determine the oxygen consumption by individual tissues. A study of the intensity of tissue respiration (on 34 rats) showed that among the tissues



Tissue Pressure of Oxygen (pO_2) and Carbon Dioxide (pCO_2) in mm Hg in Norm and in Hypokinesia
On x-axis--days of experiment, on y-axis--tissue pressure of oxygen and carbon dioxide in mm. White columns--pCO_2, hatched--pO_2.

TABLE 2

INTENSITY OF TISSUE RESPIRATION IN MM^3 O_2 PER 100 MG OF MOIST TISSUE IN 1 HOUR

Conventional experiments		Brain	Heart	Liver	Muscle
Control	M	78	62	85	19
	m	±4.25	±4.78	±5.98	±3.98
	n	17	17	17	17
Hypokinesia 45 days	M	85	56	131	25
	m	±7.25	±7.95	±9.97	±6.59
	p	12	12	12	12
		> 0.05	> 0.05	< 0.0001	> 0.05
Hypokinesia 60 days	M	65	38	108	17
	m	±5.72	±6.22	±11.1	±4.30
	p	5	5	5	5
		> 0.05	< 0.05	> 0.05	> 0.05

we studied the most distinct changes emerged in the liver and myocardium (table 2). Thus, O_2 consumption in the liver sections on the 45th day of hypokinesia increased to 131±9.97 mm^3 per 100 mg of moist tissue in 1 hour with 85±5.98 mm^3 in the control group ($d<0.0001$). By the 60th day this intensification in respiration had become less pronounced and was 108±11.1 mm^3 O_2 ($d>0.05$). In the myocardium the opposite results were obtained. Here already in 45 days a tendency was discovered for decrease in O_2 absorption, and on the 60th day of hypokinesia--a considerable statistically reliable attenuation in respiration (38±6.22 mm^3 per 100 mg of moist tissue in 1 hour, with 62±4.78--in the control, $d<0.05$). In the tissues of the brain and skeletal muscle in 45 and 60 days from the beginning of hypokinesia no distinct changes were observed in the intensity of respiration.

In the later studies on tissue pastes incubated in a medium containing oxidation substrates (succinate and α-ketoglutarate) the same laws were obtained. In the liver tissue the intensity of respiration rose: in one experiment by 50% (30th day of hypokinesia), and in another by 63% (45th day of hypokinesia, $d<0.05$). In the myocardial tissue the O_2 absorption was reduced by 17%, $d<0.05$ (60th day). /1811

Thus, the repeated experiments with prolonged limited mobility indicated that during the second month of hypokinesia periods emerge of increase in respiratory intensity in the liver and decrease of its level in the myocardium.

In addition to a study of the general and regional gas metabolism a study was also made of the energy effectiveness of the respiration according to the amytal test. However, no changes were found in the percentage correlation of amytal-resistant and amytal-sensitive respiration on the 60th day of hypokinesia. Consequently, the correlation of free and phosphorylating oxidation in the studied periods in the experimental animals remained the same as in the control. The amytal-resistant respiration in the experimental rats was 46±2.0%, in the control--45±1.8%.

The dynamics of live weight of the experimental and control animals is reflected in table 3 from which it follows that the weight of the experimental rats steadily lagged behind that of the controls. By the end of the 60th day of the experiment the weight of the control rats who were freely moving was 392±16 g, considerably surpassing the weight of the experimental rats--273±10 g.

After 60-day hypokinesia the physical endurance of the rats was sharply reduced (table 4). Changes were noted both in the dynamic and the static component of performance capacity. The duration of the maximum dynamic work was reduced by more than 2.5-fold. The ability for static work suffered even more (reduction 9-fold). These data indicate the detraining of the skeletal musculature of the animals that had gone very far in the coures of the 60 days of hypokinesia.

TABLE 3

WEIGHT OF ALBINO RATS IN 60-DAY HYPOKINESIA

Day of experiment	Control rats		Experimental rats	
	number of animals	weight of animal, in g ($\bar{x} \pm \sigma_{\bar{x}}$)	number of animals	weight of animals, in g ($\bar{x} \pm \sigma_{\bar{x}}$)
initial weight	30	274±15	48	254± 8
15	30	323±12	48	255± 6
30	30	348±16	46	261±10
45	30	380±18	39	272± 5
60	30	392±18	23	273±10

TABLE 4

MAXIMUM PHYSICAL PERFORMANCE CAPACITY OF ALBINO RATS IN 60-DAY HYPOKINESIA

Physical endurance	Control animals	Animals after 60-day hypokinesia
Maximum duration of limit dynamic work (swimming test), in seconds ($\bar{x} \pm \sigma_{\bar{x}}$)	191±0.37	76±0.10
Maximum duration of limit static work (vertical rod), in seconds ($\bar{x} \pm \sigma_{\bar{x}}$)	k83±0.57	20±0.02

Thus, the conducted studies demonstrated that 60-day hypokinesia does not produce significant changes in the general gas metabolism and pressure of oxygen and carbon dioxide in the tissues. However, respiration of individual tissues is altered: in the second month of hypokinesia periods are revealed of increased intensity of respiration in the liver and decreased in the myocardium. Concerning the reasons for these shifts one can hypothesize that an intensification in respiration of the liver cells probably is induced by a dominance in this period of hypokinesia of catabolic processes over anabolic [6]. And the low level of respiration of the cardiac muscle is linked to the detraining of the myocardium with its transition to a new, lower level of functioning under conditions of reduced motor activity. /1812

The most drastic disruptions in our experiments were observed in the functional activity of the skeletal musculature (sharp reduction in the performance capacity) and in the physical development of the animals, which was manifest in the slowing down in the rates of growth in the weight of

the animals. The lag in weight of the animals indicates a disruption in the plastic metabolism and is evidently linked to the disruption in protein synthesis [7].

Conclusions

1. Sixty-day hypokinesia does not have a significant effect on the general gas metabolism and intratissue gas homeostasis.

2. Prolonged hypokinesia produces changes in the intensity of tissue respiration: intensification in respiration in the liver and attenuation in the myocardium (on the 45th and 60th days).

3. Physical performance capacity of the animals after 60-day hypokinesia is reduced several times.

4. Sixty-day hypokinesia produces a considerable delay in the weight increase of the animals.

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